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OCA PAD AMENDMENT - PROJECT HEADER INFORMATION

04/16/91

Active

Project #: G-33-662 Cost share #:
Center # : 10/24-6-Q5384-3A0 Center shr #:
Contract#: 5 R01 EY07006-04 Mod #: REV NOA 4/12/91
Prime #: Document : GRANT
Contract entity: GIT

Subprojects ? : N
Main project #:

Project unit: CHEMISTRY Unit code: 02.010.136
Project director(s):
YU N-T CHEMISTRY (404)894-4007

Sponsor/division names: DHHS/PHS/NIH / NATL INSTITUTES OF HEALTH
Sponsor/division codes: 108 / 001

Award period: 900401 to 920331 (performance) 920630 (reports)

Sponsor amount	New this change	Total to date
Contract value	0.00	114,429.79
Funded	0.00	114,429.79
Cost sharing amount		0.00

Does subcontracting plan apply ? : N

Title: CLINICAL MONITOR OF DIABETIC LENSES BY FLUORESCENCE

PROJECT ADMINISTRATION DATA

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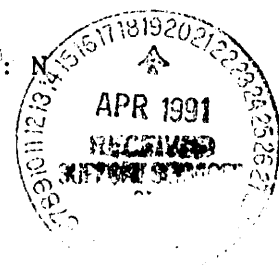
NATL EYE INST, NATL INST OF
BLDG. 31, ROOM 6A48
BETHESDA, MD 20894

Security class (U,C,S,TS) : U
Defense priority rating :
Equipment title vests with: Sponsor

ONR resident rep. is ACO (Y/N): N
NIH supplemental sheet
GIT X

Administrative comments -

ISSUED TO EXTEND TERMINATION DATE FROM 3/31/91 TO 3/31/92.



GEORGIA INSTITUTE OF TECHNOLOGY
OFFICE OF CONTRACT ADMINISTRATION

NOTICE OF PROJECT CLOSEOUT

Closeout Notice Date 06/22/92

Project No. G-33-662_____

Center No. 10/24-6-Q5384-3A0_

Project Director YU N-T_____

School/Lab CHEMISTRY_____

Sponsor DHHS/PHS/NIH/NATL INSTITUTES OF HEALTH_____

Contract/Grant No. 5 R01 EY07006-04_____ Contract Entity GIT_

Prime Contract No. _____

Title CLINICAL MONITOR OF DIABETIC LENSES BY FLUORESCENCE_____

Effective Completion Date 920331 (Performance) 920630 (Reports)

Closeout Actions Required:	Y/N	Date Submitted
Final Invoice or Copy of Final Invoice	N	_____
Final Report of Inventions and/or Subcontracts	Y	_____
Government Property Inventory & Related Certificate	N	_____
Classified Material Certificate	N	_____
Release and Assignment	N	_____
Other _____	N	_____

Comments_____

Subproject Under Main Project No. _____

Continues Project No. G-33-686_____

Distribution Required:

Project Director	Y
Administrative Network Representative	Y
GTRI Accounting/Grants and Contracts	Y
Procurement/Supply Services	Y
Research Property Management	Y
Research Security Services	N
Reports Coordinator (UCA)	Y
GTRC	N
Project File	Y
Other _____	N
_____	N

NOTE: Final Patent Questionnaire sent to PDPI.

633-602

**Final Report
of
NIH project: 5 R01 EY07006-04**

This progress report covers the period from June 1, 1990 to March 31, 1992.

Measurements have been made from the lenses of 85 patients with Type I Diabetes Mellitus (DM) at an excitation wavelength of 406.7 nm and 117 patients at an excitation wavelength of 441.6 nm. Measurements at the 406.7 nm excitation have also been made from 43 patients with Type II DM and 18 age matched non-diabetic subjects. These later measurements from Type II patients were performed through an undilated pupil.

Measurements have also been performed using excitation wavelengths of 488 and 514 nm from an air cooled Argon laser which was incorporated into the measurement system. A total of 26 diabetic subjects and 10 non-diabetic subjects have been measured at these excitation wavelengths. Figure 1 a-d illustrate lens fluorescence spectra obtained from the nucleus of a 33 year old Type I diabetic patient (duration 8 years) at the 4 different excitation wavelengths used.

We have also conducted a pilot study in collaboration with Dr. L.T. Chylack and Dr. J. Liang using 31 enucleated eyes obtained from the National Disease Research Interchange (NDRI). The aim of this study was to investigate possible correlations between clinical lens gradings, lens fluorescence measurements and lens protein fractions using the same lenses.

Analysis of the results using the patient data accumulated at the 406.7 and 441.6 nm excitation wavelengths was performed using the fluorescence/Rayleigh line (F/R) ratios obtained from the lens nucleus. Figure 2 a, b illustrate the data obtained at 406.7 nm. In this case it is evident that, at a fixed excitation wavelength, normalized lens fluorescences calculated as the F/R ratio provided a more sensitive discrimination between diabetic and non-diabetic lenses (Fig 2a) than the more traditional total lens fluorescence measurements (Fig 2b). Thus this method of analysis facilitates a quantitative investigation of more specific lens fluorophor species by restricting excitation to a single wavelength and restricting the resulting measured intrinsic fluorescence to a 10 nm wavelength band about the wavelength at which the peak spectral fluorescence intensity occurs.

A significant relationship between F/R ratio and age was demonstrated at the 406.7 nm excitation wavelength for non-diabetic subjects (Fig 3). The data at this wavelength, for both diabetic and non-diabetic subjects, indicated that the F/R ratio increased with age up to approximately age 50, while lenses older than age 50 showed little change with age. In contrast, the results at 441.6 nm excitation (Fig 4) showed little change with age in lenses younger than age 30 and increasing F/R ratios with increasing age in the older subjects. This would suggest that there may be a conversion

of the shorter excitation wavelength (406.7 nm) lens fluorophor species to species with excitation wavelengths showing greater efficiencies at longer excitation wavelengths (441.6 nm) as the lens ages.

The results at the 406.7 nm excitation wavelength were also correlated with Hemoglobin A1c levels or average glycemic control. Figure 5 illustrates the relationship between increasing A1c levels and age corrected increasing F/R ratios. The age correction was implemented using the age relationship in Fig 3. The solid line is the result of the regression analysis demonstrating a significant relationship with a correlation coefficient of 0.9. Thus at the 406.7 nm excitation wavelength there appears to be a significant association between the average level of glycemic control and increased lens fluorescence.

The study on Type II diabetic patients was performed using only the 406.7 nm excitation wavelength. The measurements were performed through the undilated pupil and measurements were restricted to just the one excitation wavelength in order to facilitate a faster measurement time and better patient compliance. The aim of the study was to investigate whether the same degree of F/R ratio discrimination was attained in a population of Type II DM patients as was observed in the Type I patients. The results from these measurements did not demonstrate the same degree of discrimination as that seen in Type I patients. Thus while on average the diabetic patients had higher F/R ratios, the difference between the diabetic patients and the age matched controls was not remarkable. It was felt that this observation may be due to the fact that the ages of the Type II patients were all over 50 years and in an age range where there may have been conversion of this fluorophor to longer wavelength species and where we had previously observed little change in F/R ratios with age, at this excitation wavelength. Measurements were then extended to include excitation wavelengths of 441.6 and 488 nm. Preliminary results at these excitation wavelengths demonstrate, on average a factor of 2 greater F/R ratios in the diabetic lenses than the non-diabetic lenses. if these results are consistent, then it is anticipated that these measurements could be used to non-invasively screen populations for detecting possible undiagnosed Type II diabetes. These results have provided the basis for a SBIR application through Laser Atlanta.

The pilot study aimed at investigating possible correlations between F/R ratios, clinical lens color evaluations and extracted protein fluorescences were performed using enucleated eyes obtained from NDRI. The age range of these 31 eyes was between 65 and 101 years.

Color photographs of these lenses were taken after removal of the corneas. These photographs were analyzed for color purity using the LOCS-II grading protocols. lens fluorescences were then measured at excitation wavelengths of 406.7 nm and 441.6 nm. The use of longer excitation wavelengths was not possible at the time

of this study as the Argon laser had not been ordered. Following lens fluorescence measurements, the lenses were removed from the globe, frozen at -20°C and lens proteins were subsequently extracted for analysis. The excised lenses were decapsulized, homogenized and the resulting protein separated into its water soluble and insoluble components. Non-tryptophan fluorescence was measured from these fractions. The results from these measurements indicated that at the 406.7 nm excitation there was no significant association with any of the other measured parameters. At the 441.6 nm excitation, however, there was a significant association between F/R ratios and lens purity evaluated at the lens nucleus ($p=.044$) and with both the water soluble and water insoluble lens protein fractions ($p=.04$). The lack of association between F/R ratios at 406.7 nm excitation and lens color or non-tryptophan fluorescence is probably a reflection of the lack of change with age of this particular fluorophor in the older lenses studied here.

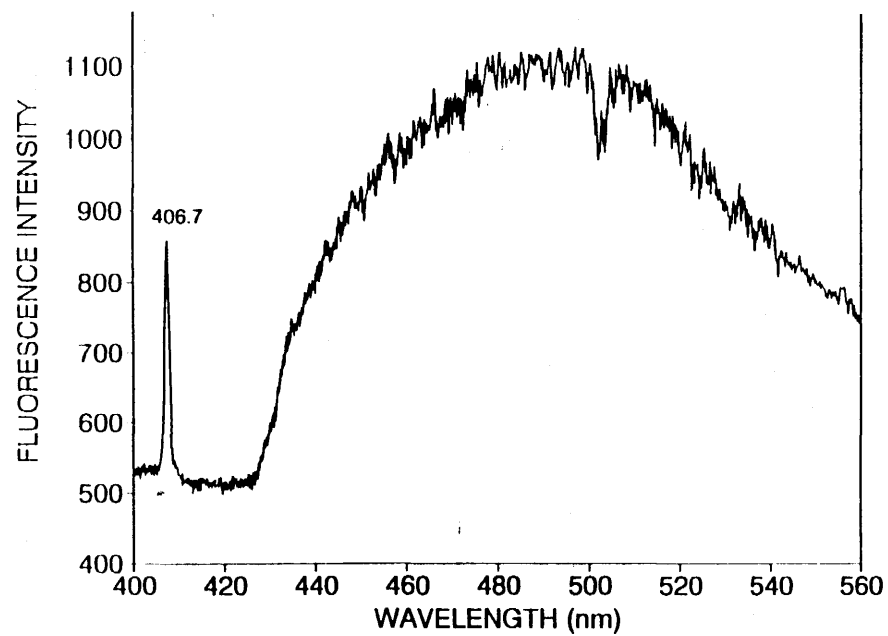


FIGURE 1a

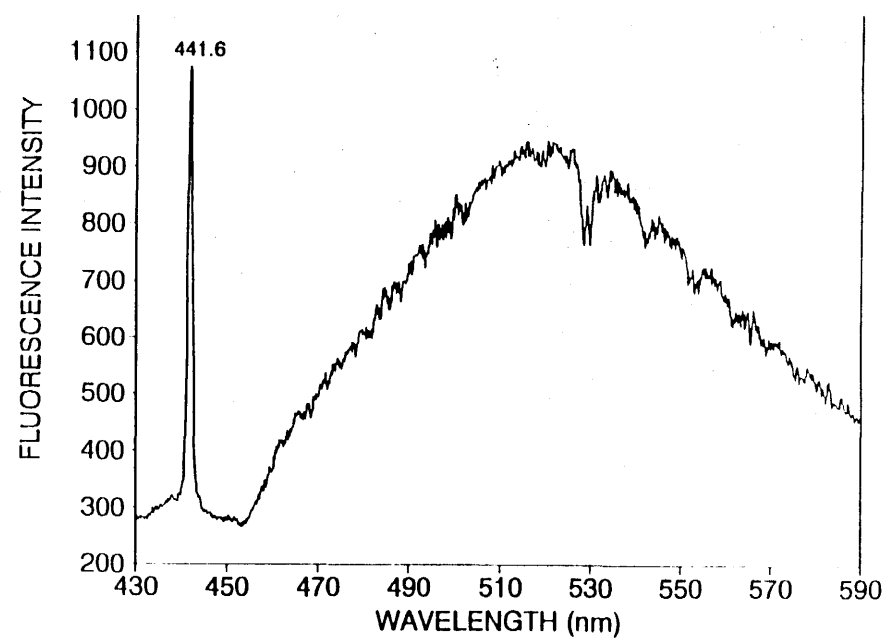


FIGURE 1b

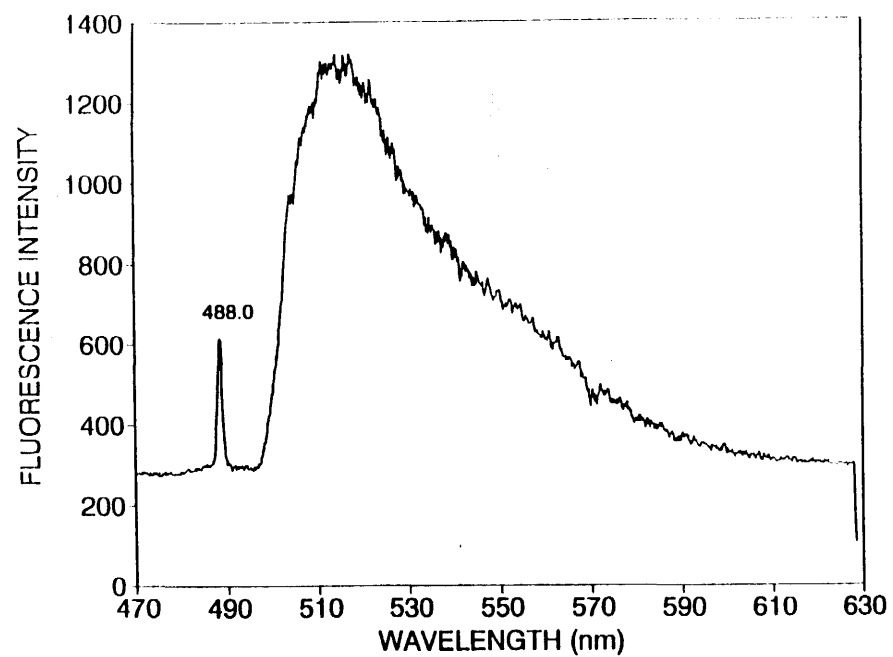


FIGURE 1c

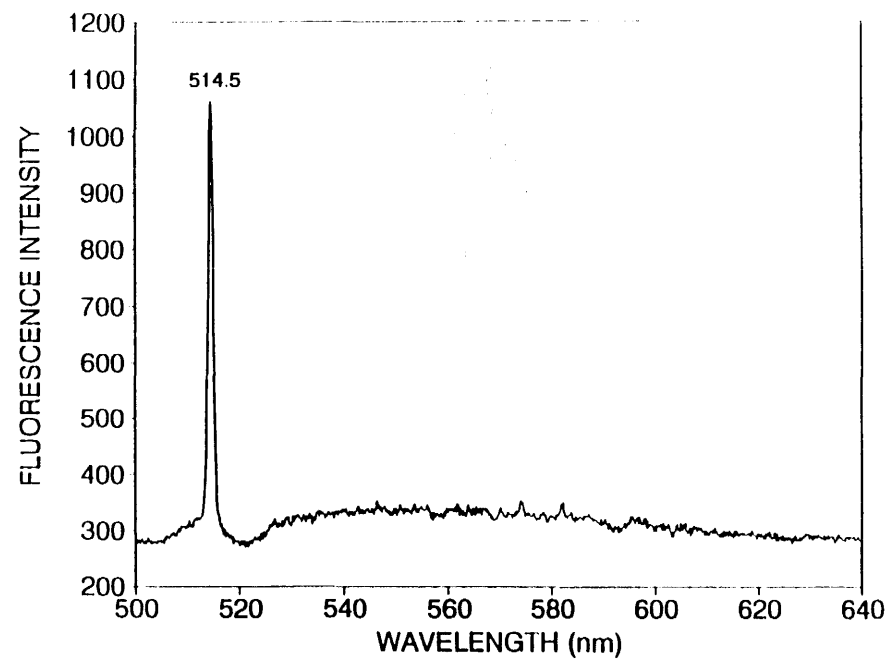


FIGURE 1d

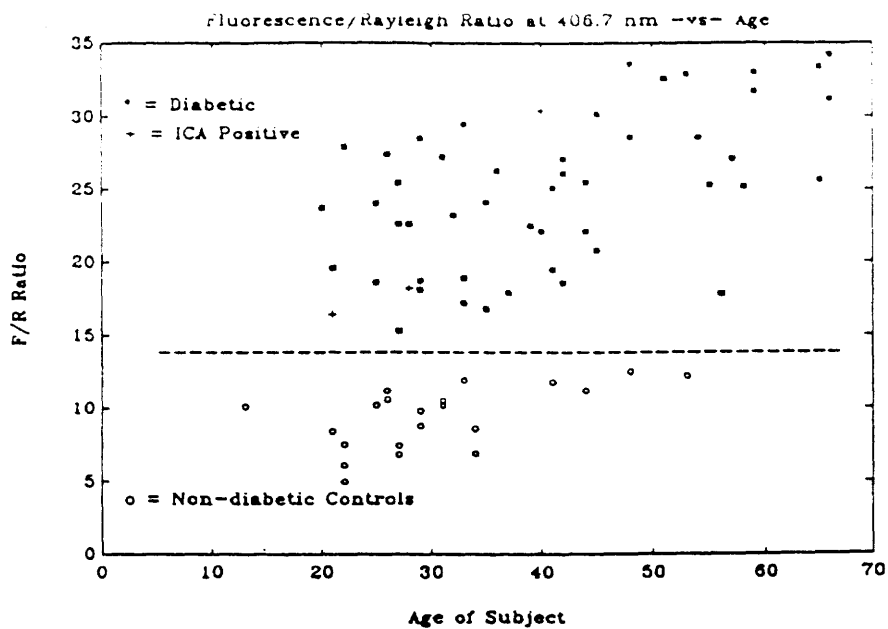


FIGURE 2a

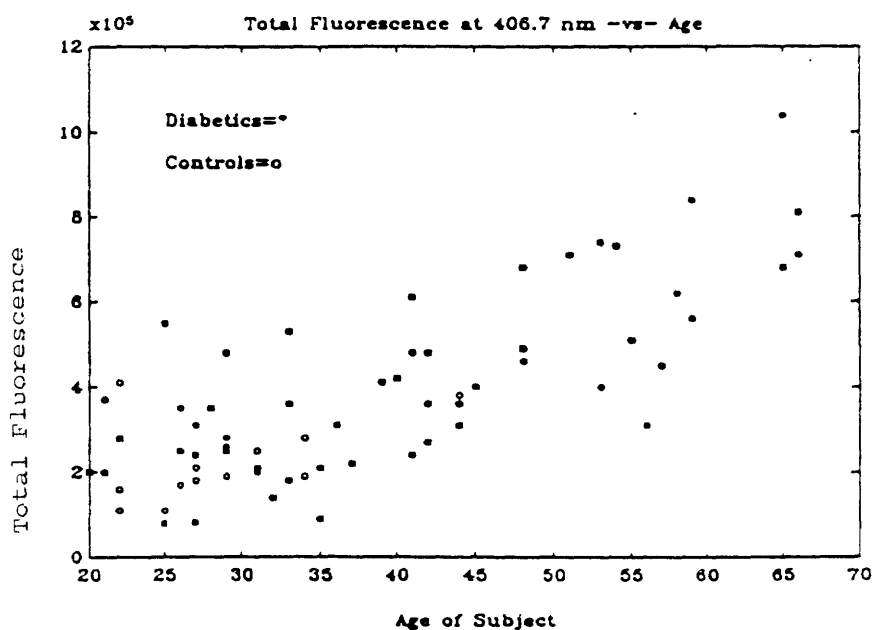


FIGURE 2b

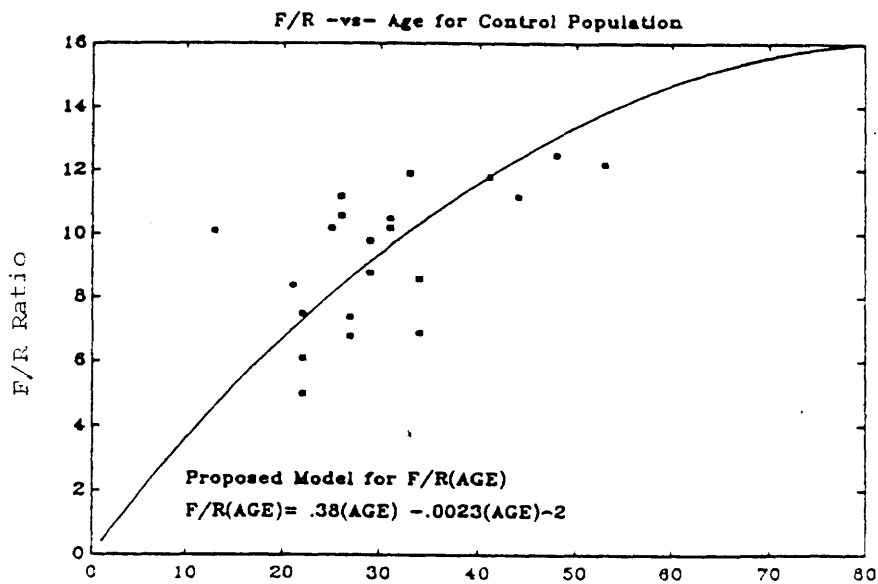


FIGURE 3

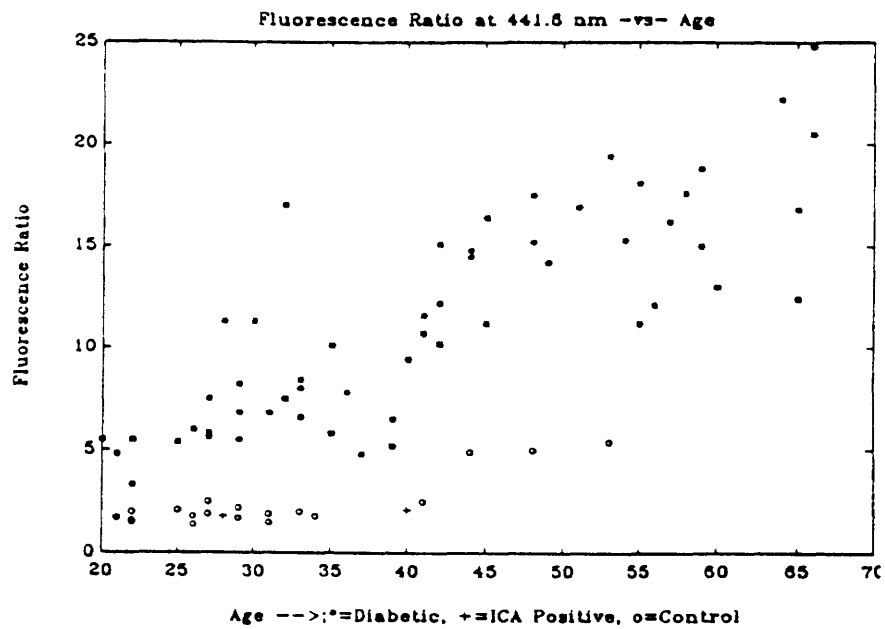


FIGURE 4

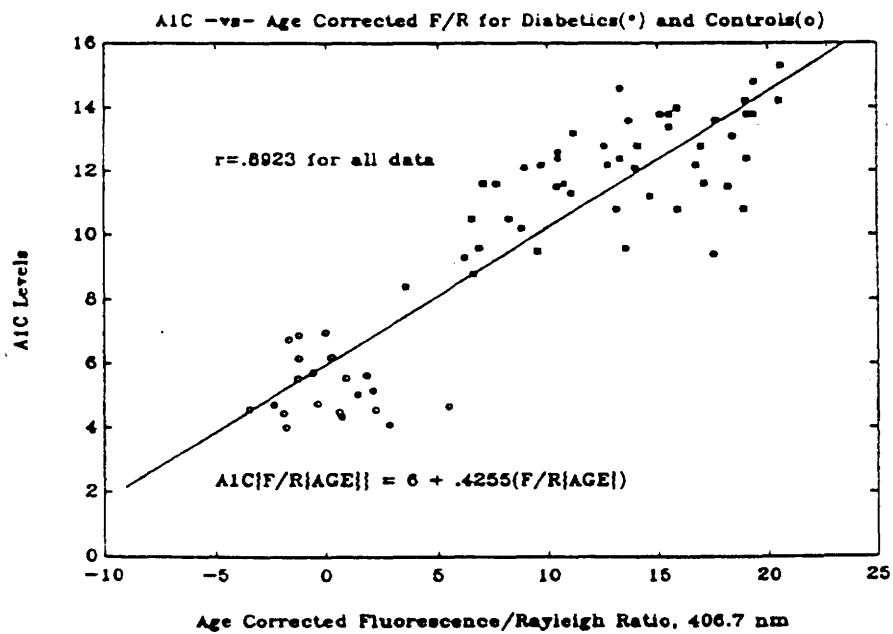


FIGURE 5